REMARKS

Applicants thank Examiners Joyce and Ungar for their time during the telephonic interview of May 31, 2006. During the interview, attended in the WSGR offices by Russell Boggs, Jeff Guise, and Shannon Kenealy, the rejections encompassed by the pending office action were discussed. Applicants agreed that in the event allowable subject matter was obtained, Applicants would submit the required declarations regarding the deposit of cell lines expressing RM2 and RM4 to address part of one of the enablement rejections. Applicants and Examiners also discussed the scope of the pending claims and Applicants agreed to focus the claims on the use of RM4 and RM2 to treat lung cancer and colon cancer. Applicants agreed to submit draft claims; Applicants submitted a first and second set of draft claims.

Applicants further thank Examiner Joyce for a follow-up interview on June 19, 2006 in which the draft claims focused on the treatment of lung cancer and colon cancer were discussed. Attending the interview were Examiner Joyce and Russell Boggs. Applicants agreed to submit claims similar to the second set of draft claims in an amendment to be filed on or before July 3, 2006.

Claims 53-83 are pending. Claims 54, 55, 58, 63, 68, 73, and 74 are canceled to expedite prosecution. Claims 53, 62, 67, 82 and 83 are currently amended. Support for the amendments can be found throughout the specification. Applicants reserve the right to pursue any canceled subject matter in continuation or divisional applications.

Sections 1, 2, and 3

Applicants thank the Examiner for entering the restriction requirement and species election and proceeding with the examination of claims 53-83.

Section 4

The Examiner has rejected 82 under 35 U.S.C. § 112, first paragraph, as being indefinite by failing to particularly point out and distinctly claim the subject matter regarded as the invention, The Examiner has drawn our attention to the phrase "an antibody" in claim 82 and

stated that it is unclear what type of antibody is being claimed. Applicants respectfully suggest that the rejection no longer applies to the claim as amended. Antibodies displaying therapeutic activity with respect to cancer are disclosed in both the Background section and at page 26, lines 7-17.

Sections 5 and 6

The Examiner has rejected claims 53-83 under 35 U.S.C. § 112, first paragraph, as not being enabled in such a way as to enable one of skill in the art to make and/or use the instant invention.

The Examiner summarized the reach of the pending claims as regards in vivo inhibition. The Examiner stated that the claims are drawn to:

(i) a method of inhibiting or preventing the proliferation of a cell that expresses AgRM4 comprising contacting the cell with an amount of an isolated human monoclonal antibody that is designated RM4 and that selectively binds an antibody designated RM4 (claims 53-61);

(ii) a method of treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, the isolated human monoclonal antibody that is designated RM2 and that selectively binds to an antigen designated AgRM2, or the antibody that is designated RM4 and the antibody that is denoted RM2 (claims 62-66); and

(iii) a method treating a subject having or at risk of having a tumor comprising administering to the subject an amount of the antibody designated RM4 that selectively binds to an antigen designated AgRM4 (claims 67-82), wherein the method may also comprise administering RM2 (claim 83).

After summarizing the claimed invention, the Examiner stated that it is unclear whether the cell lines that can produce the RM2 antibody ("RM2") and the RM4 antibody ("RM4") are

publicly available or known, or whether they could be reproducibly isolated without undue experimentation. Without the cell lines, the Examiner stated that it would be difficult to practice the instant invention as claimed. The Examiner suggests a suitable deposit for patent purposes. The Examiner noted the disclosure in the specification, such as on page 2 at lines 14-18, that a deposit has been made. The Examiner noted that this disclosure, in and of itself, is insufficient as there is no proof that the deposits have been made and further that the requirements of MPEP 608.01 (p)(c) have not been met.

Applicants draw the Examiner's attention to the attached receipt from the ATCC acknowledging the deposit of cell lines PTA-5411 and PTA-5412 under the terms of the Budapest Treaty. Applicants will, if a patent issues with claims directed to the antibodies RM2 and/or RM4, remove all restrictions to the public's access to the above-referenced deposited cell lines.

If allowable claims result from prosecution of the instant application, Applicants will submit an affidavit or declaration that a deposit of these cell lines was made under the terms of the Budapest Treaty, that the deposit was accepted by an International Depository Authority under the terms of the Treaty, that Applicants will replace the deposited cell lines if the cell lines no longer produce viable samples, and that all restrictions on the public availability of the deposited material will be irrevocably removed upon the granting of a patent in the United States.

The Examiner also brings to Applicants' attention MPEP1.804(b). The attached receipt shows a deposit date of of August 22, 2003. In the event claims are allowed, applicants plan to submit a statement that the deposited biological material is the biological material specifically identified in the application as filed.

Section 7

Claims 53-83 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph. The Examiner stated that the specification is enabling for methods of:

(i) inhibiting or preventing the proliferation of a cell that expresses AgRM4 comprising contacting the cell with an amount of an isolated human monoclonal antibody that is

designated RM4 and that selectively binds an antibody designated RM4 wherein the cells are colon cancer cells or lung cancer cells;

(ii) treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, wherein the hyperproliferative disorder is lung cancer or colon cancer; and

(iii) treating a subject having or at risk of having a tumor comprising administering to the subject an amount of the antibody designated RM4 that selectively binds to an antigen designated AgRM4, wherein the tumor is a lung tumor or a colon tumor.

However, the Examiner stated that the specification does not reasonably provide enablement for:

(i) a method of inhibiting or preventing the proliferation of a cell that expresses AgRM4 comprising contacting the cell with an amount of an isolated human monoclonal antibody that is designated RM4 and that selectively binds an antibody designated RM4,

(ii) a method of treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, and

(iii) a method treating a subject having or at risk of having a tumor comprising administering to the subject an amount of the antibody designated RM4 that selectively binds to an antigen designated AgRM4.

The Examiner further noted that claims 53-61 read on both in vitro as well as in vivo inhibition of proliferation/cancer cell treatment.

The Examiner then summarized the enablement requirement of § 112 as set forth in the Federal Circuit's decision In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The Examiner summarized the reach of the pending claims as regards in vivo inhibition. The Examiner stated that the claims are drawn to:

(i) a method of inhibiting or preventing the proliferation of a cell that expresses AgRM4

comprising contacting the cell with an amount of an isolated human monoclonal antibody that is designated RM4 and that selectively binds an antibody designated RM4 (claims 53-61);

(ii) a method of treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, the isolated human monoclonal antibody that is designated RM2 and that selectively binds to an antigen designated AgRM2, or the antibody that is designated RM4 and the antibody that is denoted RM2 (claims 62-66); and

(iii) a method treating a subject having or at risk of having a tumor comprising administering to the subject an amount of the antibody designated RM4 that selectively binds to an antigen designated AgRM4 (claims 67-83).

The Examiner summarized the teachings of the specification and the reactivity of the RM4 and RM2 antibody with regards to normal tissue and cancer tissue. The Examiner noted how the human monoclonal antibody RM4 was isolated and converted into a hybridoma. The Examiner also noted that RM4 is reactive with breast, colon, gastric, and lung cancer cell lines, as well as breast, colon, and lung tumor tissue, but not reactive with normal tissues. The Examiner also noted that the specification teaches that immunohistochemistry analysis indicates that the RM2 antibody is reactive with breast, lung, melanoma, pancreatic tumor tissue but not reactive with normal tissues. The Examiner also noted that RM4 is effective in causing tumor regression in mice injected with human colon cancer cell line Colo205, and that the combination that RM4 with RM2 is synergistically effective in causing tumor regression in mice injected with human lung cancer cell line Calu1. The Examiner also noted that when treatment with RM4 is stopped, Colo205 tumor growth progressed rapidly.

The Examiner asserted that the teachings of the specification cannot be reasonably extrapolated to read on:

(i) methods of inhibiting or preventing the proliferation of all cells that express AgRM4,

including all cancer cells,

(ii) methods of treating a hyperproliferative disorder, wherein at least a portion of the cells express AgRM4, wherein the hyperproliferative may be any hyperproliferative disorder; or

(iii) a method of treating a subject having or at risk of having a tumor, wherein the tumor may be any tumor.

The Examiner stated that one cannot extrapolate the teaching of the specification to the scope of the claims because one cannot predict that contacting any type of cell that expresses the AgRM4 with the RM4 antibody would be effective in inhibiting or preventing the proliferation of cells, except for the colon cancer and lung cancer cell lines of the working examples.

To support the argument that the teachings of the specification cannot be reasonably extrapolated to all cancer cells, the Examiner cited to Busken et al., a study finding a difference in COX-2 expression in adenocarcinomas of the cardia and distal esophagus. The Examiner argued that it cannot be predicted that the invention will function as claimed in the inhibition of cell types other than colon cancer or lung cancer because of because of the heterogeneity of all cancers with respect of levels of antigen expression and localization. Thus, the Examiner argued, even if the AgRM4 antigen is expressed on cancer cells or hyperproliferating cells, other than cells of colon or lung cancer, the specification does not provide any guidance on whether the antigen is present in sufficient concentration on other cancer cell types or hyperproliferating cell types to allow for successful therapeutic targeting of the AgRM4 antigen or inhibition of cell growth.

The Examiner also cited to a review by White et al. that describes the characteristics of an ideal antigen for immunotherapy. White et al. discuss characteristics of a preferred antigen target, assuming specificity of the antibody for the antigen: first, whether or not the antigen is present on all or nearly all malignant cells, and second, whether the antigen is shed, modulated, or internalized. The Examiner argued that the specification does not provide guidance as to whether AgRM4 may be shed, modulated or down-regulated by cells to be targeted.

The Examiner next discussed the therapeutic antibody trastuzumab (Herceptin®), and

cited to a French protocol of treatment for trastuzumab in adjuvant conditions. The Examiner argued that the critical nature of antigen presentation is well understood in the art as demonstrated by the treatment of breast cancer with the therapeutic antibody trastuzumab where it has been demonstrated that patients can benefit from treatment with trastuzumab if they exhibit strong overexpression of HER-2. Applicants agree with the Examiner in so far that the protocol suggests that it is possible to successfully inhibit the growth of cancer cells with an antibody if said cancer cells express the antigen recognized by the antibody. Applicants note that the French treatment protocol clearly indicates that it is within the skill of an artisan to screen a prospective patient's cancer for expression of an antigen prior to treatment, in this case, HER-2. Thus, treatment with a therapeutic antibody could readily limited to those patients expressing the relevant antigen without undue experimentation.

The Examiner concluded that given the heterogeneity of cancer antigen presentation in the same organ based on Busken et al., given the lack of teaching drawn to intensity of antigen presentation based on White et al., and the apparent critical requirement for sufficient antigen presentation based on the French protocol for treatment with trastuzumab demonstrates when taken together that one cannot that predict that the invention will function as claimed in the in vivo inhibition of cell types other than colon cancer or lung cancer.

The Examiner further asserted that claims 67-83 encompass methods of treating a tumor wherein the tumor cells do not express the AgRM4 antigen.

The Examiner additionally asserted that claims 53-61 encompass methods of inhibiting or preventing the proliferation of a cell expressing AgRM4 in vitro by contacting such a cell with RM4 in vitro, other than lung cancer cells expressing AgRM4 or colon cancer cells expressing AgRM4.

The Examiner concluded it would require undue experimentation to practice the invention as claimed.

In order to facilitate prosecution of the instant application, Applicants have amended the claims and believe that the rejection no longer applies to the claims as amended. Applicants reserve the right to pursue any canceled subject matter in continuation or divisional applications.

Section 8

The Examiner then stated that even if the above rejection of claims 53-61 were overcome, the claims would still be rejected under 35 U.S.C. § 112, first paragraph, because although the specification is enabling for a method for inhibiting the proliferation of a cell that expresses AgRM4, it does not reasonably provide enablement for a method for preventing the proliferation of a cancer cell that expresses AgRM4. The Examiner then cited to the reoccurrence of cancer in the specification's working example following cessation of treatment. Gura (1997) is cited as an example of the unpredictability of cancer treatment. Applicants believe that the specification provides support for the treatment of cancer with RM4 in the working examples where RM4 acts to prevent the proliferation of cells during treatment.

Nevertheless, solely to facilitate prosecution of the instant application, Applicants have amended the claims and believe that the rejection no longer applies to the amended claims. Applicants reserve the right to pursue any canceled subject matter in continuation or divisional applications.

Section 9

The Examiner continued that even if the rejection of claims 62-66 discussed above was overcome, claims 62-66 would still be rejected under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for

(i) a method for treating hyperproliferative disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of RM4;

(ii) a method for treating hyperproliferative disorder, wherein at least a portion of the hyperproliferative cells express AgRM2 comprising administering to a subject an amount of RM2; and

(iii) a method for treating hyperproliferative disorder, wherein at least a portion of the hyperproliferative cells express AgRM4 AND AgRM2 comprising administering to a

subject an amount of RM4 as well as RM2,

does not reasonably provide enablement for a method for treating a hyperproliferative disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the monoclonal antibody that is designated RM2 or comprising administering to a subject the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated RM4 and the antibody denoted as RM2.

The Examiner stated that the claims in question are drawn to a method of treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, which method comprises administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, the isolated human monoclonal antibody that is designated RM2 and that selectively binds to an antigen designated AgRM2, or the antibody that is designated RM4 and the antibody that is denoted RM2.

The Examiner summarized the teachings of the specification and the reactivity of the RM4 and RM2 antibody with regards to normal tissue and cancer tissue. The Examiner noted how the human monoclonal antibody RM4 was isolated and converted into a hybridoma. The Examiner also noted that RM4 is reactive with breast, colon, gastric, and lung cancer cell lines, as well as breast, colon, and lung tumor tissue, but not reactive with normal tissues. The Examiner also noted that the specification teaches that immunohistochemistry analysis indicates that the RM2 antibody is reactive with breast, lung, melanoma, pancreatic tumor tissue but not reactive with normal tissues. The Examiner also noted that RM4 is effective in causing tumor regression in mice injected with human colon cancer cell line Colo205, and that the combination that RM4 with RM2 is synergistically effective in causing tumor regression in mice injected with human lung cancer cell line Calu1. The Examiner also noted that when treatment with RM4 is stopped, Colo205 tumor growth progressed rapidly.

The Examiner stated that the teaching in the specification does not enable the claims; specifically, the Examiner pointed out that treating a subject having a hyperproliferative disorder where those cells express AgRM4 with RM2 could not be predicted to be effective. The

Examiner underlines that the specification does not disclose any correlation between AgRM4 and AgRM2 expression. The Examiner continued the rejection and wrote:

> "[f]urther, one cannot extrapolate the teaching of the specification to the enablement of the claims because one cannot predict that the invention would function as claimed in treating a subject having a hyperproliferative disorder wherein the cells are treated with an RM4 antibody and an RM2 antibody and wherein the cells express the AgRM4 antigen but do not express the RM2 antigen. As stated above, the specification does not disclose any correlation between AgRM4 expression and AgRM2 expression. Thus, one of skill in the art could not predict that the invention would function as claimed in the treatment of hyperproliferative disorders with RM4 antibody and the RM2 antibody, wherein the cells express the AgRM4 antigen and not the AgRM2 antigen."

Applicants have redrafted claim 62 and respectfully request that the Examiner reconsider this rejection in view of the amendment. Applicants reserve the right to pursue any canceled subject matter in continuation or divisional applications.

Section 10

The Examiner continued in the Office Action by stating that even if the above rejections were overcome, claims 67-83 would still be rejected under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for treating a patient having a tumor expressing AgRM4, is not enabling for treating a subject at risk of having a tumor comprising administering an amount of RM4.

The Examiner summarized the teachings of the specification and the reactivity of the RM4 and RM2 antibody with regards to normal tissue and cancer tissue. The Examiner noted how the human monoclonal antibody RM4 was isolated and converted into a hybridoma. The Examiner also noted that RM4 is reactive with breast, colon, gastric, and lung cancer cell lines, as well as breast, colon, and lung tumor tissue, but not reactive with normal tissues. The Examiner also noted that the specification teaches that immunohistochemistry analysis indicates that the RM2 antibody is reactive with breast, lung, melanoma, pancreatic tumor tissue but not reactive with normal tissues. The Examiner also noted that RM4 is effective in causing tumor

regression in mice injected with human colon cancer cell line Colo205, and that the combination that RM4 with RM2 is synergistically effective in causing tumor regression in mice injected with human lung cancer cell line Calu1. The Examiner also noted that when treatment with RM4 is stopped, Colo205 tumor growth progressed rapidly.

The Examiner stated that the specification does not define individuals at risk of having a tumor, and there is no teaching in the specification as to when the method of treatment is to be initiated. Thus, the Examiner concluded that one cannot predict that the invention would function as claimed in treating a subject at risk of having a tumor.

The Examiner argued that the majority of the population of the United States have been exposed carcinogenic substances but that many or most of the individuals will not develop a malignancy. The Examiner argued that the existence of a genetic predisposition for developing cancer in individuals may exist, and argued that it is well-known in the art that not all of these individuals eventually develop cancer. The Examiner asserted that the identification of individuals at risk for cancer is a developing art, and cited to a 2000 summary of chronic diseases in Canada (Cotterchio et al.). The Examiner concluded that "[t]he reference clearly suggests the lack of predictability of the art when concluding that the familial history study is useful for the ***development*** (emphasis added) of chemoprevention trials."

The Examiner also cited to a 2000 study regarding risk factors and breast cancer by Apantaku, emphasizing the difficulties in identifying or altering the risk in developing breast cancer, or identifying when to begin intervention. The Examiner also cited a review by Martin et al. as stating that that cancer prevention of breast cancer is currently speculative. The Examiner concluded that given the teachings of the specification and the art of record, it is not possible to have a reasonable expectation of success in treating a subject at risk of having a tumor.

Applicants respectfully request that the Examiner reconsider this rejection with respect to claims 67-83 as amended. Applicants reserve the right to pursue any canceled subject matter in continuation or divisional applications.

Section 11

The Examiner further stated that even if the rejection of claim 83 was overcome, claim 83 would not be enabled because the specification, although enabling for a method of treating a subject having a tumor wherein the tumor cells express AgRM4 comprising administering an amount of RM4, and enabling for a method of treating a subject having a tumor wherein the tumor cells express AgRM2 comprising administering an amount of RM2, does not reasonably provide enablement for a method of treating a subject having a tumor that expresses AgRM4 comprising administering to the subject an amount of the antibody RM4 and further administering the antibody RM2.

The Examiner summarized the teachings of the specification and the reactivity of the RM4 and RM2 antibody with regards to normal tissue and cancer tissue. The Examiner noted how the human monoclonal antibody RM4 was isolated and converted into a hybridoma. The Examiner also noted that breast, colon, gastric, and lung cancer cell lines, as well as breast, colon, and lung tumor tissue, but not reactive with normal tissues. The Examiner also noted that the specification teaches that immunohistochemistry analysis indicates that the RM2 antibody is reactive with breast, lung, melanoma, pancreatic tumor tissue but not reactive with normal tissues. The Examiner also noted that RM4 is effective in causing tumor regression in mice injected with human colon cancer cell line Colo205, and that the combination that RM4 with RM2 is synergistically effective in causing tumor regression in mice injected with human lung cancer cell line Calu1. The Examiner also noted that when treatment with RM4 is stopped, Colo205 tumor growth progressed rapidly.

The Examiner concluded that "[o]ne cannot extrapolate the teaching of the specification to the scope of the claims because one cannot predict that the invention would function as claimed in treating a subject having a tumor wherein the cells are treated with an RM4 antibody and an RM2 antibody and wherein the cells do not express the AgRM2 antigen."

Therefore, Applicants respectfully request that the Examiner reconsider this rejection in view of the claims as amended.

Section 12

The Examiner concluded the office action by rejecting claims 53-66 as lacking adequate written description requirement under 35 U.S.C. § 112, first paragraph. The Examiner summarized the pending claims as being drawn to the following inventions:

> (i) a method of inhibiting or preventing the proliferation of a cell that expresses AgRM4 comprising contacting the cell with an amount of an isolated human monoclonal antibody that is designated RM4 and that selectively binds an antibody designated RM4 (claims 53-61),
>
> (ii) a method of treating a hyperproliferative cell disorder, wherein at least a portion of the hyperproliferative cells express AgRM4, comprising administering to a subject an amount of the isolated human monoclonal antibody that is designated RM4 and that selectively binds to an antigen designated AgRM4, the isolated human monoclonal antibody that is designated RM2 and that selectively binds to an antigen designated AgRM2, or the antibody that is designated RM4 and the antibody that is denoted RM2 (claims 62-66).

The Examiner based this rejection on two cases normally associated with the DNA arts, Regents of the University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002).

The Examiner pointed out that in these cases the Federal Circuit addressed the application of the written description requirement to DNA-related inventions. The Examiner quoted Lilly: "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Lilly at 1567, 43 USPQ2d at 1405. The Examiner continued by quoting the passage:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One

> skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. at 1568, 43 USPQ2d at 1406.

(emphasis omitted). The Examiner continued, quoting "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Lilly at 1568, 43 USPQ2d at 1406.

The Examiner quoted from the next page of the decision where the court addresses the manner in which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Lilly at 1569, 43 USPQ2d at 1406.

The Examiner then reviewed the decision of Enzo and quoted the standard set forth that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . .i.e., complete or partial structure, other physical andlor chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.' Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original)."

The Examiner then argued that although the inventions at issue in Lilly and Enzo were DNA constructs, the holdings of those cases are also applicable to the pending claims.

The Examiner focused on the limitations: "a cell that expresses AgRM4" or of "a hyperproliferative disorder, wherein a portion of the hyperproliferative cells express AgRM4" and stated that the holding in Lilly requires a representative number of species of "a cell that expresses AgRM4" or species of "hyperproliferative disorder, wherein a portion of the hyperproliferative cells express AgRM4" or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." The

Examiner continued that as an alternate means of satisfying the written description requirement under Enzo, the specification is required to "[disclose] sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

The Examiner then stated that the specification, in light of the holdings of Lilly and Enzo, does not describe "a cell that expresses AgRM4" or of "a hyperproliferative disorder, wherein a portion of the hyperproliferative cells express AgRM4" other than the expression of the AgRM4 antigen in breast, lung, melanoma, and pancreatic primary cancer cells with no expression in normal tissue and in breast, and expression of the antigen in breast, lung, colon, and gastric cell lines. The Examiner also concluded that although the specification described expression of AgRM4 in breast, lung, melanoma, and pancreatic primary cancer cells, and breast, lung, colon, and gastric cell lines, this description does not satisfy the standard of Enzo.

The Examiner further stated that the specification fails to satisfy the standard set forth in Lilly. The Examiner argued that although the specification described expression of the AgRM4 antigen in all the above-referenced cells, it has failed to describe a "representative number" of such species. Additionally, the Examiner stated that the specification does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the Examiner concluded that the specification does not provide an adequate written description of "a cell that expresses AgRM4" or of "a hyperproliferative disorder, wherein a portion of the hyperproliferative cells express AgRM4.

Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

The MPEP states that "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.'" MPEP 2163.01 (citing In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)).

One of ordinary skill in the art is able to practice the invention as currently claimed given the disclosure in the specification. One of ordinary skill in the art is interested in treating cancer

using the antibody provided by the invention. The specification describes both the antibodies to be used in the claimed methods, RM4 and RM2 and how to obtain them via the deposited cell lines. These antibodies also provide a means of identifying target cells expected to be recognized by RM4 and RM2. From the French protocol for trastuzumab therapy cited by the Examiner, it is apparent that it is well within the reach of those of ordinary skill in the art to screen possible cancer patients for the expression of a relevant antigen prior to treatment. Thus, the specification complies with the written description as set forth in the MPEP.

Therefore, Applicants respectfully request the Examiner to reconsider and withdraw this rejection in view of the claims as amended.

CONCLUSION

Applicants believe that for the reasons set forth above, the Examiner's rejections of the claims are overcome. Applicants respectfully request allowance of the pending claims.

The two-month extended deadline for filing a response falls on July 3, 2006. Applicant submits herewith a two-month Petition for Extension of time and the appropriate fee. Therefore, Applicants believe that this response is being timely filed. However, in the event that Applicants are incorrect in their assumption, please charge any fee due to Deposit Account No. 23-2415, referencing Docket No. 31302-702.201.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2309.

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Russell T. Boggs, Reg. No. 55,011

Date: June 30, 2006

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ATCC

10801 University Blvd. • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.

To: (Name and Address of Depositor or Attorney)

SHANTHA WEST, Inc.
Attn: Mark C. Glassy
1121 Sorrento Valley Road
Suite C
San Diego, CA 92121

[redacted]

Deposited on Behalf of: SHANTHA WEST, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
Human hybridoma: RM2	PTA-5411
Human hybridoma: RM4	PTA-5412

The deposits were accompanied by: __ a scientific description , a proposed taxonomic description indicated above. **The deposits were received** August 22, 2003 **by this International Depository Authority and have been accepted.**

AT YOUR REQUEST: X **We will inform you of requests for the strains for 30 years.**

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested September 4, 2003. **On that date, the cultures were viable.**

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris

Marie Harris, Patent Specialist, ATCC Patent Depository **Date:** September 29, 2003

cc: John Wetherell

BP4/9

ATCC

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10801 University Boulevard
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FAX

To:	Mark Glassy
Company	SHANTHA WEST Inc.
Fax No:	858-658-9230
# of Pages	2 (Including Cover Sheet)
From:	Marie Harris
E-mail:	mharris@atcc.org
Date:	September 19, 2003
Reference:	Lab copy of PCR Results - Patent Deposit PTA-5411 (RM2) and PTA-5412 (RM4)

COMMENTS:

Attached is the lab copy of the results of PCR test on your material submitted for patent deposit purposes on August 22, 2003 for your information only.

Thank you

Marie Harris

Marie Harris

ATCC

Mycoplasma Detection

PCR REPORT for

Customer Name: Farah Haq Order Number: in-house

	Customer Designation	ATCC Code	Amplified Product Detected[3]
A	NONE	Positive Control	yes
B	NONE	Negative Control	no
1	PTA-5411	C2	no
2	PTA-5412	C3	no
3	[redacted]	[redacted]	[redacted]
4			

3) This test is performed pursuant to licensing arrangements with Roche Molecular Systems, Inc. and Applied Biosystems. A positive report indicates detection of amplified DNA in the 200 – 400bp size range. A negative report indicates that there was no amplified DNA detected in the 200 – 400bp size range. Some samples are reported as needing further study to confirm initial results. Final results will be reported the following week.

DNA harvested from the above listed samples has been subjected to amplification by PCR using primers provided in the ATCC's Mycoplasma Detection Kit. These primers readily produce DNA fragments of characteristic size when the primers are allowed to amplify DNA from cultures containing *Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. pirum, M. salivarium,* and *Acholeplasma laidlawii* as well as many other species of Mollicutes. While the primers exhibit excellent specificity, production of DNA amplicons in the 200-400bp size range from other prokaryotes such as certain strains of Lactobacillus, and Chlamydia has been observed. The primers may also amplify mycoplasma-specific DNA fragments from mycoplasma that have been inactivated by treatment with solvent, or other technique that leaves the mycoplasma DNA intact.

COMMENTS

Callope Sarago	Biologist	9/12/03
Signature	Title	Date

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